ABSTRACT OF THE DISCLOSURE

The method is used for separating nucleic acids and other similar constructs. It involves selective introduction, enhancement, or stabilization of affinity handles such as single-strandedness in the undesired (or desired) nucleic acids as compared to the usual structure (e.g., double-strandedness) of the desired (or undesired) nucleic acids. The undesired (or desired) nucleic acids are separated from the desired (or undesired) nucleic acids due to capture by methods including but not limited to immobilized metal affinity chromatography, immobilized single-stranded DNA binding (SSB) protein, and immobilized oligonucleotides. The invention is useful to: remove contaminating genomic DNA from plasmid DNA; remove genomic DNA from plasmids, BACs, and similar constructs; selectively separate oligonucleotides and similar DNA fragments from their partner strands; purification of aptamers, (deoxy)-ribozymes and other highly structured nucleic acids; Separation of restriction fragments without using agarose gels; manufacture recombinant *Taq* polymerase or similar products that are sensitive to host genomic DNA contamination; and other applications